

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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Applicant : David R. Hennings et al.
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Docket No. : 15487.4002
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DECLARATION OF MITCHEL P. GOLDMAN, M.D.

1. I am one of the named inventors in the above-identified application.
2. I am also one of the named inventors in United States Patent No. 6,258,084.
3. I was consulted by VNUS Medical Technologies, Inc. because of difficulties they had encountered with the Radio Frequency (RF) technology for treating varicose veins described in Zikorus Patent No. 7,676,433, which difficulties included lack of efficacy.
4. I had, prior to working with VNUS, successful experience in using tumescent anesthesia in ambulatory phlebectomy procedures, as described in *Phlebectomy, A Practical Guide for Treating Varicose Veins*, by Ricci, Georgiev and Goldman (Mosby 1995), which is Exhibit 1 hereto, and in Smith & Goldman *Tumescent Anesthesia in Ambulatory Phlebectomy, Dermatological Surgery*, 1998, 24:453-456 and Keel and Goldman, *Tumescent Anesthesia in Ambulatory Phlebectomy: Addition of Epinephrine, Dermatological Surgery*, 1999, 25:371-372, which are attached hereto as Exhibits 2 and 3.

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5. The work upon which my Patent No. 6,258,084 is based involved only the use of tumescent anesthesia in the RF treatment of varicose veins and no work of any sort was done involving the use of lasers. Prior to filing the application which became Patent No. 6,258,084, we had no experience or knowledge which would permit us to enable the use of lasers to treat varicose veins. For example, we did not know which laser wavelengths might be useful nor did we know what power levels might be safe and effective.

6. To the best of my knowledge, it was not until the laser treatment technology for varicose veins described in Navarro Patent No. 6,398,777 was developed that a first actual attempt to treat varicose veins endoluminally with lasers was made. None of the laser technology disclosed in the Navarro Patent was known to or considered by us when we did the work on RF treatment described in Patent No. 6,258,084. Furthermore, this first attempt by Navarro took the wrong path by electing to use laser wavelengths in the range of 500-1100 nm. Prior to the invention claimed in the present application all other workers following Navarro used laser wavelengths within the range disclosed by Navarro, typically within the range of 810-1064 nm and wavelengths of 810 nm and 980 nm were among those used.

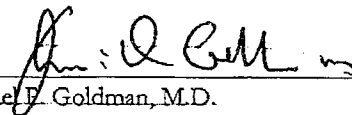
7. As disclosed in the present application, wavelengths in the range of 500-1100 nm target blood as a chromophore and thus heat the blood which then heats the vessel wall by conduction and convection. In contrast, the invention claimed in the present application which used wavelengths of 1200 to 1800 nm, and preferably 1320 nm, target the water in the vessel wall and thus heat the vessel wall directly rather than indirectly. In addition, Navarro considered it necessary for the fiber optic which delivered the laser energy to make direct contact with the vein wall whereas such direct contact is not necessary when practicing the invention of the present application.

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8. Our use of laser wavelengths in the range 1200-1800 nm as claimed in the present application was contrary to the view held by prior art workers that such wavelengths would be undesirable, a view expressed in the Min and Proebstle articles which are attached to the Geriak Declaration as Exhibits A, B and C and which are representative of the belief held by the prior art prior to the invention claimed in this application.

Further, Declarant sayeth not.

I declare under penalty of perjury that the foregoing is true and correct. Executed this 23
day of December, 2008 at La Jolla, California.



Mitchell E. Goldman, M.D.

EXHIBIT 1

EXHIBIT 1

AMBULATORY PHLEBECTOMY

A Practical Guide
for Treating Varicose Veins

Stefano Ricci, M.D. and Mihael Georgiev, M.D.

with Mitchel P. Goldman, M.D.

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Preface

During the last century, long saphenous vein (LSV) ligation and stripping (L&S) has been (and still is) such a common operation for varicose veins that it has become synonymous with varicose vein surgery. This has occurred despite evidence that the "prefabricated" stripping operation, based on textbook anatomy, poorly matched the clinical variability of varicose vein disease. In fact, L&S is appropriate and successful in only some cases, since in many others it leaves the collateral varicose veins untreated. There are cases in which it is not even indicated, since 20% to 30% of the limbs with varicose veins may not have an incompetent LSV.¹⁻³ Though possible to perform on patients who are under local anesthesia and on an outpatient basis, L&S of the LSV is almost always performed on patients who are under general or regional anesthesia.

The inadequacy of the stripping operation noted in the 1940s and the 1950s stimulated the development of sclerotherapy by Sigg in Switzerland,⁴ Tournay in France,⁵ Fegan in Ireland,⁶ and Orbach in the United States.⁷ Though some schools propose sclerotherapy as an alternative to the stripping operation, the optimal use of sclerotherapy is to complement the treatment of the collateral varicose veins not removed by the stripping operation.

Sclerotherapy is a versatile office procedure. Theoretically, any varicose vein, including telangiectasias, can be injected. In expert hands the treatment is safe and the results excellent. However, long-term results of sclerotherapy are conditioned by a variable rate of recanalization in treated veins.⁸⁻¹⁵

In the 1950s, Robert Muller, a Swiss dermatologist, developed a technique for varicose vein avulsion through multiple stab incisions and called it "la phlebectomie ambulatoire." Muller designed his own instruments and reported that his procedure was appropriate for treating all varicose veins with the exception of an incompetent saphenofemoral junction.¹⁶⁻²⁰ This technique permits removal of any varicose vein (except telangiectasias and the proximal portion of the LSV with the saphenofemoral junction) in an office setting and on patients who are under local anesthesia. The Muller technique is often referred to as "stab avulsion," "office phlebectomy," and "ambulatory stab avulsion phlebectomy." Only within the last decade have physicians recognized that it represents a major improvement in varicose vein surgery. This technique achieves the long-term results of surgical treatment with less inconvenience, lower cost, and better cosmesis than traditional surgical treatment or combination surgery/sclerotherapy. However, over 30 years after its introduction and despite recent interest, ambulatory phlebectomy is still discussed more often than practiced. This may be due to the lack of a textbook describing the technique in detail. Our goal is to fill this gap. We believe that, especially for a manual technique, "details make the master;" we learned this from our teachers and from the experience of the colleagues who visit our practice.

Although the description of ambulatory phlebectomy techniques is essential, it is more important to determine the proper method of treatment for each type of varicose vein. This statement is controversial, since the technique can be employed in two different (and in a sense, opposite) ways. The first is to employ it complementary to traditional surgery for the removal of the collateral varicose veins left

after the stripping operation. The second is for removal of all varicose veins, thus limiting traditional surgery to only high ligation and division of the LSV. Although the objectives of varicose vein surgery can be achieved by both approaches, we propose the latter choice, which is described in this text.

Not all varicose conditions can be treated with ambulatory phlebectomy; venous telangiectasias are best treated with sclerotherapy, whereas LSV incompetence is best treated with high ligation, division, and stripping of the proximal LSV portion. To provide a complete practical guide for office-based surgical treatment of varicose veins, our technique for L&S of the LSV is also described.

This book is not a textbook of phlebology. The physiology, pathology, investigation, and diagnosis of the venous disorders of the lower limb, as well as the available wide range of surgical, nonsurgical, and sclerotherapy procedures, are not discussed here. Those who need or wish to improve their knowledge on these and other topics should turn to other sources, some of which are listed at the end of this section.

We hope this text is useful for those who wish to include ambulatory phlebectomy in their phlebological practice. The techniques described in this text are personal. However, we have attempted to separate the essential points from the many personal details, which in our hands are useful but not mandatory. We tried to create a text that might trigger an "imaginary movie" in the reader's mind; it is the reader who will judge how well we succeeded.

Among those who contributed to the realization of this book, our special thanks go to Dr. Mitchel Goldman. His contribution goes far beyond the revision of the manuscript and the additions the reader will find throughout the text. Were it not for his enthusiastic encouragement and support at the very beginning of our work, this project would have not been realized.

S. Ricci
M. Georgiev

Preface

The treatment of venous disease in the United States has been undergoing a rapid evolution during the past decade. This was primarily stimulated by the popularization of sclerotherapy for the treatment of varicose and telangiectatic leg veins. However, it soon became apparent that many veins, especially those larger than 6 to 8 mm in diameter and those with reflux from various junctions, were better treated with surgical techniques. This led to an improvement and enhanced cosmesis of the traditional ligation and stripping procedures. In addition, the American physician has once again borrowed concepts developed by our European colleagues to modify the stripping part of the surgical procedure into one of stab avulsion or ambulatory phlebectomy. It is therefore fitting that a textbook on this technique be made available for the English-speaking physician.

My personal instruction in ambulatory phlebectomy has come from observation of many of my European colleagues. In this regard, Gerhard Sattler, Alina Fratila, and Jacques Dortu have been very illustrative. However, by far the greatest instruction I have received is from Mihael Georgiev. It is therefore a privilege to be asked by Drs. Ricci and Georgiev to review and revise their text, *Ambulatory Phlebectomy*, to present it to the American reader. This outstanding text gives an excellent step-by-step description with copious illustrations of the technique of ambulatory phlebectomy by stab avulsion. It primarily represents the considerable experience of Drs. Ricci and Georgiev. Deviations from their explicit technique have been added (italicized) where appropriate in the various chapters. In addition, a separate section regarding administration of anesthetic has also been added to better reflect the standard of care of the American physician. Where technical details and materials differ from current U.S. standards for dermatologic and vascular surgery, these have been commented on throughout the text. This will hopefully offer the reader a stimulus to broaden his or her approach to the technique and modify the technique to fit personal standards.

In Europe, there are hundreds of phlebologists who have considerable experience performing phlebectomy. There are national societies of phlebectomy, and even a European society. Naturally, there are many different types of instruments, including hooks, forceps, ministrippers, and dissectors, which have been specifically developed for this technique. Although all these variations work and some may have unique advantages over the teaching in this text, an extensive discussion of each technique is beyond the scope of this book. The purpose of this book is thus to educate the physician on the technique perfected by Drs. Ricci and Georgiev. As I have done, the reader is then urged to modify the numerous techniques to customize this procedure for his or her practice.

M.P. Goldman

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Anesthetic



Section I: Ricci-Georgiev Method*

PREPARATION AND DOSAGE

Local infiltration anesthetic (LA) is administered exclusively along the course of the marked varicose veins. Anesthesia is performed with 0.4% mepivacaine (or other suitable local anesthetic) with 1:500,000 epinephrine in saline, neutralized with 40 to 60 mEq/L of sodium bicarbonate to reduce the pain of injection.^{1,2,3} If this solution is not available, the proper concentration must be prepared by dilution of a commercial solution. We dilute 4 ml of 2% mepivacaine/1:100,000 epinephrine solution (available in Italy in 20 ml vials) with 12 ml of saline and 4 ml of 1.4% sodium bicarbonate, obtaining 20 ml of neutralized 0.4% mepivacaine/1:500,000 epinephrine solution. This solution is injected at body temperature (37° C) instead of room temperature for further reduction of pain as suggested in a recent report.⁴ To attain approximately 37° C we heat the saline and bicarbonate solutions to 50° C and then add the anesthetic. The preparation of the anesthetic solution employed is illustrated in Table 7-1, page 72. (Many authors, on the contrary, refrigerate the anesthetic solution to reduce pain. However, it is not clear why refrigerated solution should be less painful, and this practice is not validated by objective studies.)

In our hands the 0.4% solution proved to be the lowest efficacious concentration, but both lower⁶ and higher^{5,7} concentrations are employed by others. About 0.5 ml of LA per cm is sufficient, though larger amounts may be necessary if a larger and/or deeper infiltration is needed (e.g., for large, tortuous, multiple, or deeper varicose veins). Usually 20ml of 0.4% solution is sufficient for a 20 to 40 cm strip of vein.

We employ an average of 20 to 40 ml (80 to 160 mg mepivacaine) for each session and limit the extension of phlebectomy accordingly. This is less than one third the recommended maximum dosage for mepivacaine, which is 550 mg (or 7 mg/kg).⁸ An exception is in LSV high ligation with groin to knee stripping, for which 320 mg may be necessary (see Chapter 15). However, there is evidence that even larger doses are safe. In a recent study it was found that during phlebectomy under LA with 600 mg or more of lidocaine (8 to 15 mg/kg) (18 patients), the serum level of lidocaine was in average 0.6 µg/ml with a maximum of 1.8 µg/ml in one patient only. This maximum is still less than one half the concentration considered neurologically toxic (4 to 12 µg/L) and less than one twelfth the concentration considered toxic to the cardiovascular system (24 µg/L).⁵

TECHNIQUE

The pain of LA injection is due more to infiltration than to needle puncture. LA injection is therefore less unpleasant when the needle is small and infiltration slow. We perform LA injection with a 20 ml eccentric cone disposable syringe and 2 cm long, 27 gauge needle (Terumo 27 gauge, 0.4 × 20 mm). This needle exerts moderate resistance to injection so that infiltration is slower and less painful. It also permits optimal control of the injected amount of anesthetic. With

*Section I written by Stefano Ricci and Mihael Georgiev.

Table 7-1 Preparation of the anesthetic solution: dose for one syringe (20 ml) of anesthetic.

Mepivacaine 2% with epinephrine 1:100,000	4 ml
Sodium bicarbonate 1.4%	4 ml
Saline, warmed at about 50° C	12 ml

larger needles, injection is inevitably faster and more painful, and anesthetic is wasted because amounts larger than necessary are injected.

Though infiltration of neutralized and warmed LA is almost painless, it is still the most uncomfortable part of the procedure and is the one with which the invasive part of the treatment begins. Therefore it is important to perform injection in the most painless and comfortable manner since this will reassure the patient and make him or her more relaxed and cooperative. For this purpose, conversing with the patient in a warm and interested manner is of great help and has a positive psychological effect no medication can match.

The patient is placed in a slight Trendelenburg position (head down-foot up tilt) to avoid emotional vagal reactions. The extension of surgery and anesthetic is decided, and the skin is prepared with a suitable surgical disinfectant. The first injection must be announced to avoid surprise and possible defensive reaction. Perception of pain and reaction to it vary from patient to patient; individual reaction is evaluated during the first injection, and infiltration is then slowed or accelerated as needed.

Superficial (intradermal and subdermal) infiltration is sufficient unless there are deep trunks (e.g., in surgery of the thigh portion of the LSV, large perforators, or the saphenofemoral or saphenopopliteal junction), in which case deeper infiltration may be necessary.

Injection begins immediately after the insertion of the tip of the needle and proceeds as the needle is pushed forward. If the needle is in the perivenous space, LA often dissects it, infiltrating a tunnel that may extend a few centimeters beyond the tip of the needle; a longitudinal wheal and/or bleaching results and is clearly visible (Fig. 7-1). In such a case the next injection is made at the end of the wheal, which is longer than the needle's length, so that fewer injections are needed.

Aspiration to check for intravenous position of the needle is usually unnecessary. Correct position is recognized by wheal formation. Moreover, the small diameter of the needle, its continuous movement, and the slow rate of injection make an accidental IV injection of a large amount of LA unlikely. On the contrary, aspiration is performed when deep (perpendicular) infiltration is needed (e.g., in the groin).

When infiltrating a long and straight segment, we start injecting from the middle (or from a bifurcation) and then proceed alternatively in both (or more) directions. Next injections are made from areas that are already anesthetized. Thus needle insertion is not averted by the patient, and the pain of infiltration is reduced. Not all areas of the limb are equally sensible to LA infiltration. Injection is more painful on the foot and medial knee, where it should be slower, and is practically painless in the groin.

At the end of infiltration the anesthetized skin appears pale due to epinephrine-induced vasoconstriction. However, it is useful to test the effectiveness of the anesthetic with a second series of injections, injecting more anesthetic

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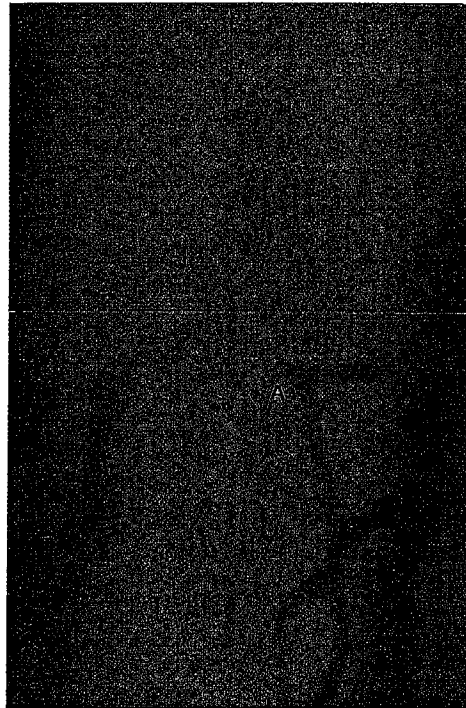
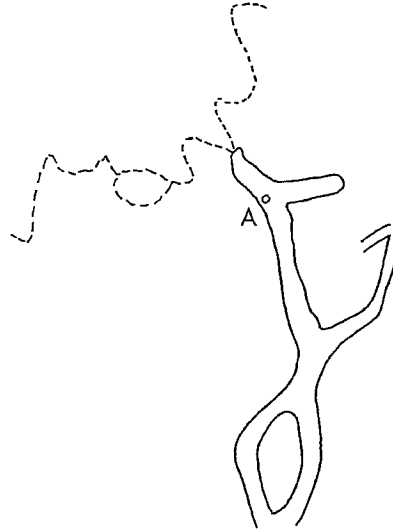


Fig. 7-1 Anesthesia administered with epinephrine-containing solutions causes vaso-
spasm, evidenced as skin blanching over the marked vessel. If infiltration is performed in
the perivenous cleavage plane, the anesthetic solution may spread for many centimeters
further along the vein as seen by blanching beyond the injection site (A).

if needed. Mepivacaine LA reaches maximum strength in 10 to 15 minutes and lasts 2 to 3 hours. It is advisable to keep a syringe of LA ready in case supplementary infiltration is needed during surgery (e.g., in case of insufficient initial dose, errors in marking, unexpected collaterals, deviations in the course of the marked veins, or bad diffusion of LA due to cicatrix tissue).

For LA administered as previously described, such a low dose of mepivacaine/epinephrine is employed that there are few contraindications. However, it is possible in special cases (e.g., in elderly patients who are unable to maintain the needed position) to limit the extension of surgery per session and thus employ a very low (40 to 80 mg) dose of LA.

In other cases (e.g., in patients who have diabetes, glaucoma, coronary heart disease, cardiac arrhythmias, arterial hypertension, hyperthyroidism, or advanced occlusive arterial disease) mepivacaine may be employed without epinephrine. Unlike other local anesthetics, mepivacaine does not cause vasodilation; on the contrary, it even causes some vasoconstriction. It is therefore more suitable for use without epinephrine than are other local anesthetics. However, when using mepivacaine without epinephrine, the surgeon must expect (besides more bleeding) major and more rapid anesthetic absorption and shorter duration of anesthesia.

At the dose employed by us, adverse reactions to LA are exceptionally rare and mild. It has been calculated that more than one million ambulatory phlebectomies have been performed in Europe without a single major accident.⁹ This is because adverse reactions to LA are dose-dependent, and it has been shown that systemic concentrations of the anesthetic during anesthesia for phlebectomy are much lower than those advised.⁵ However, the surgeon must be able to promptly recognize and adequately treat any untoward reaction that appears. Adverse reactions to LA and their diagnoses and treatments are discussed in Chapters 16 and 19.



Section II: Goldman Method*

PREPARATION AND DOSAGE

Local infiltration anesthetic (LA) is administered exclusively along the course of the marked varicose veins. Anesthesia is performed with 1% lidocaine with 1:100,000 epinephrine diluted 1:10 with bacteriostatic normal saline. This solution is injected at body temperature (37° C) instead of room temperature for further reduction of pain as suggested in a recent report.¹⁻⁴

We employ an average of 60 to 160 ml for each session and limit the extension of phlebectomy accordingly. Using this quantity of anesthetic is essentially an adaptation of the tumescent technique for liposuction surgery, which has been described by Klein.¹⁰ The benefits of the tumescent technique are most likely due to extensive diffusion throughout subcutaneous and adipose tissues through the use of large volumes of fluid. A mechanical effect from the pressure generated by engorging fatty tissue with the anesthetic solution may also result in enhanced anesthesia. Both the volume and pressure used result in a thorough permeation of even the smallest capillaries and nerve endings.¹¹ The anesthetic effect of this dilute lidocaine mixture in subcutaneous fat has been shown to persist for as long as 16 hours postoperatively. Therefore supplemental postoperative analgesia usually is not necessary.

Although the tumescent technique was originally developed for use in lipo-

TECH

*Section II written by Mitchel P. Goldman.

suction surgery, its use has been expanded for scalp surgery, dermabrasion, and soft tissue reconstruction.¹²

We prefer lidocaine as the drug of choice for dermatologic surgery and tumescent anesthesia, because other anesthetic agents are more likely to produce cardiovascular toxicity.¹³ However, lidocaine toxicity may occur when plasma concentrations exceed 5 mEq/ml. The use of tumescent anesthetic requires fewer total milligrams of lidocaine to achieve comparable or superior anesthesia, therefore limiting its toxicity.^{3,14} Klein recommends a maximum dose of 35 mg/kg when the tumescent technique is employed in liposuction surgery.¹¹ For nerve blocks and infiltration local anesthesia, the *Physicians' Desk Reference* and the Xylocaine (lidocaine hydrochloride, Astra Pharmaceutical Products, Inc., Westboro, Massachusetts) package inserts state, "For normal healthy adults, the individual maximum recommended dose of lidocaine HCL with epinephrine should not exceed 7 mg/kg of body weight, and in general, it is recommended that the maximum total dose not exceed 500 mg."¹⁵ However, neither the initial manufacturer of lidocaine nor the United States Food and Drug Administration has data to support this recommended maximum safe dose.¹¹ Klein has estimated that the maximum safe dose of lidocaine using the tumescent technique is 35 mg/kg. This would be equivalent to 2000 mg in a 57 kg (125 lb) patient and 2500 mg in a 73 kg (160 lb) patient.¹¹ He has shown that the use of diluted lidocaine delays absorption. In addition, slow infiltration prevents rapid lidocaine absorption. Therefore if the surgeon uses large volumes of lidocaine, it is recommended that the anesthetic be infused over 30 to 40 minutes. Typical volumes used for phlebectomy procedures are low and can therefore be infused safely over 5 to 10 minutes.

Although a diluted lidocaine mixture is extremely safe, lidocaine toxicity can occur with rapid injection of concentrated solutions. Initial clinical stages of lidocaine toxicity are lightheadedness, euphoria, restlessness, and drowsiness, which appear with levels of 3 to 6 µg/ml. Objective toxicity occurs with doses of 5 to 9 µg/ml and is seen as nausea, vomiting, tremors, blurred vision, tinnitus, confusion, excitement, psychosis, and muscular fasciculations. Doses over 8 to 12 µg/ml may lead to seizures, cardiorespiratory depression, coma, respiratory arrest, and cardiac standstill.¹¹

Diseases or drugs that decrease lidocaine metabolism may accentuate the development of lidocaine toxicity. Patients with liver disease have a decreased metabolism of lidocaine.¹⁶ Lidocaine metabolism may be diminished indirectly by diseases that diminish hepatic perfusion, such as heart disease.¹⁷ Several drug interactions can occur to either decrease lidocaine metabolism or decrease hepatic flow. The most common drugs associated with these interactions include cimetidine, beta-adrenergic receptor blockers, phenytoin, and procainamide.¹⁸⁻²⁴

TECHNIQUE

Preoperative anesthetic: Preoperative analgesia is often not necessary, especially with motivated patients. However, I routinely recommend the use of flurazepam hydrochloride (Roche Products, Inc., Manati, Puerto Rico), and suggest that 30 mg be taken the evening before the surgery. This tends to limit preoperative anxiety, which may occur in even the most cooperative of patients. To further reduce the incidence of cutaneous infection, cefadroxil monohydrate (Mead Johnson Laboratories, Evansville, Indiana) 500 mg po is given 30 to 60 minutes before the procedure and is continued bid for 3 days. In patients who are still moderately anxious before surgery, diazepam (Roche Products, Inc., Manati, Puerto Rico), 5 mg is given sublingually 30 minutes before the infiltration of anesthetic. When a

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long length of varicose vein or an extensive number of multiple clusters is to be excised, it is sometimes helpful to premedicate the patient with meperidine hydrochloride (Sanofi Winthrop Pharmaceutical, New York), 50 to 75 mg IM, combined with promethazine hydrochloride (Wyeth-Ayerst Laboratories, Philadelphia), 50 mg IM. This preoperative intramuscular "cocktail" is usually given 15 to 30 minutes before administering the infiltrative anesthetic. We recommend appropriate respiratory and cardiac monitoring when this form of intramuscular and sublingual conscious sedation is used.

Local infiltration of the anesthetic solution is then performed as previously described in Section I of this chapter.

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EXHIBIT 2

EXHIBIT 2

Tumescent Anesthesia in Ambulatory Phlebectomy

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MITCHEL P. GOLDMAN, MD

BACKGROUND. Ambulatory phlebectomy is an elegant outpatient procedure for the removal of varicose veins. One of the keys to its success is the ability to perform the procedure under local anesthesia. A new form of anesthesia, tumescent anesthesia, has been developed for liposuction surgery and is now being expanded for use in other surgical disciplines.

OBJECTIVE. To determine the efficacy and safety as well as review the use and advantages of tumescent anesthesia in ambulatory phlebectomy.

METHODS. A retrospective review of phlebectomy cases performed in our offices under tumescent anesthesia.

RESULTS. The reported level of intraoperative and postoperative pain was very low. The complication rate was consistent with other reports except for a higher number of hematomas (3.4%).

CONCLUSIONS. Tumescent anesthesia provides a very safe, comfortable method of anesthetizing patients for ambulatory phlebectomy. Epinephrine, in appropriate concentrations, should be a part of all tumescent anesthetic solutions used for phlebectomy as it may decrease the incidence of hematoma. © 1998 by the American Society for Dermatologic Surgery, Inc. *Dermatol Surg* 1998;24:453-456.

Ambulatory phlebectomy was re-introduced into the US in the 1980s.¹ Since that time it has become widely utilized as an effective, cosmetic, yet minimally invasive method of eliminating varicose veins. We have employed the tumescent technique for local anesthesia for our phlebectomy cases. This technique, originally described and developed for liposuction, may offer improved anesthesia along with several intraoperative advantages in phlebectomy.^{2,3}

In order to determine the degree of comfort offered by this technique, as well as ensure a good safety record, we conducted a retrospective review of our last 100 cases with respect to complications and patient tolerance of the procedure. Ninety-two cases had sufficient follow-up to form the basis of our evaluation.

Materials and Methods

Data Collection

Cases from June 1995 to March 1997 were analyzed. Chart notes and operative reports were reviewed for complications, total volume, and type of anesthesia used. Telephone interviews were conducted and patients were asked to rate the pain, both intraoperatively and postoperatively. A zero to five scale was used, with zero being no pain whatsoever and 5 being "severe pain but not the worst pain ever experienced."

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Anesthesia and Phlebectomy

After standing for 10 minutes to allow lower extremity veins to fill, patients were marked for surgery with a semi-permanent marker. The patient was then remarked in the supine or prone position with the Venoscope transilluminator (Applied Biotech Products, Lafayette, LA) in a darkened room. When discrepancies arose, anesthesia placement and incisions for phlebectomy were based on markings made with the transilluminator. The patient was placed in the Trendelenburg position with 10 degrees of declination. The limb was then prepped with 10% povidone-iodine solution and draped in the usual sterile manner. Some patients were given IV midazolam 0.5-3 mg if anxious. Appropriate monitoring was used.

The anesthetic solution was comprised of 0.2% lidocaine in normal saline solution buffered with 1 mEq of NaHCO₃ per 100 cc of solution. No epinephrine was used. Solutions were made using single use vials of lidocaine and stock IV solutions. Infiltration was performed with 3-inch spinal needles from 22 to 25 gauge. Anesthetic solution was delivered with 60-cc syringes or using a peristaltic pump (Wells-Johnson Company, Tucson, AZ). Care was taken to keep infiltration rates below 150 cc/min. The needle was introduced into the perivenular space and infiltration begun. During infiltration the needle was advanced as the subcutaneous space filled, and the location of the needle tip was changed often to prevent prolonged, inadvertent intravascular administration. Infiltration was completed when the area became firm or hard to the touch or the overlying skin developed a peau de orange appearance.

Phlebectomy was then performed in the usual manner using number 11 blades for microincisions and a

Table 1. *Complication Rates*

Superficial phlebitis: 0%
Blisters: 1.8%
Telangiectasias: 1.8%
Dysesthesia: 1.8%
Erosions: 1.8%
Hematoma: 3.5%
Hyperpigmentation: 3.6%

variety of hooks and dissectors to facilitate vein removal. When large perforating veins or branches were encountered the stump was tied using 3-0 polygalactin-9 suture. The incisions were bandaged with self-adhesive strips and the limb was wrapped with gauze padding and short stretch elastic bandages. Patients were seen 1-2 days postoperatively and the elastic bandages replaced with a 40-mm Hg graduated compression stocking.

Results

Women outnumbered men by more than five to one (78 to 14). The average age at time of surgery was 48 years. Follow-up periods ranged from 3 to 36 months with an average of 18 months. Seventy-one telephone interviews were completed (76%).

The volume of anesthetic fluid ranged from 100 to 700 cc, with an average of 263 cc of fluid resulting in an average dose of 528 mg of lidocaine.

The number and rate of complications is shown in Table 1. Hematomas occurred in four patients. One was a male who failed to comply with the postoperative instructions and resumed lower extremity weight lifting 48 hours after surgery. The resulting hematoma was drained and healed without complications. The three other hematomas all involved patients in whom a portion of the greater saphenous vein (GSV) was removed by phlebectomy. All were small, self-limited, and required no intervention. The rates of other complications compare favorably with other reports.^{4,5}

The average reported intraoperative pain for all interviewees was 1.0. Sixty-one of 71 interviewees (86%) rated their intraoperative pain at a two or lower. For postoperative pain, patients reported a similar degree of pain (average of 1.0), with 59 of 71 (83%) respondents reporting pain rated less than three.

No patient reported signs or symptoms of lidocaine toxicity including but not limited to agitation, circumoral paresthesias, somnolence, tremulousness, or palpitations. Plasma lidocaine levels were not studied. No cases of partial motor nerve paresis were noted.

Discussion

The development of tumescent anesthesia is generally credited to Dr. Jeffrey Klein, a dermatologist looking for

ways to improve the technique of liposuction.⁶ It began with simple local anesthesia and dilution to allow larger areas to be anesthetized without exceeding the published maximal dose of lidocaine for local infiltration. The dilution of lidocaine had a surprising effect, however. As the concentration was lowered, the anesthetic effect actually improved until a threshold of about 0.04% was reached. After large volumes of dilute anesthetic were administered, concerns arose over the blood levels of lidocaine that patients were being exposed to. It was then recognized that when lidocaine is given in this dilute, subcutaneous route that only slow, gradual elevations in plasma lidocaine levels were seen. This gave way to questioning and then exceeding the published maximal doses for lidocaine when given for local infiltration.⁷ Further documentation and now years of safe use have made it the standard for anesthesia in liposuction surgery.

The induction of any anesthesia should have safety as its primary concern. For this reason, we examined the complications found in our cases to determine whether this form of anesthesia put patients at any greater risk. We discovered a higher than expected rate of postoperative hematoma formation. This may be due to several factors. The obvious first implicated source may be only lack of operator skill. Another possible explanation is the higher proportion of cases in our series in which a portion of the GSV was removed (27%; data not shown). Conceivably, the larger vessel size would increase the likelihood of significant postoperative hemorrhage and subsequent hematoma formation. The ultimate concern, however, is that this may be some effect attributable to the anesthetic technique.

It should be noted that the anesthetic fluid used did not contain epinephrine. Early consultation with surgical colleagues convinced us not to use epinephrine for concerns of toxicity given the large volumes of anesthetic sometimes used. Subsequent to the findings of this study we have re-introduced epinephrine into the anesthetic fluid. This may decrease the incidence of hematoma formation. More importantly, it may be a crucial component of the tumescent technique by limiting lidocaine absorption. Studies of liposuction cases using lidocaine and epinephrine have shown that when very dilute lidocaine is infiltrated into the subcutaneous space, amounts are slowly absorbed and peak levels are achieved much later than would be expected with "typical" local infiltration.² This is thought to occur partly because of the dilute nature of the solution but also due to the prolonged vasoconstrictive effects seen with epinephrine. Without epinephrine, vessels are more vasodilated, anesthesia wanes more quickly, and lidocaine enters the bloodstream more rapidly. Thus, a more sudden, dramatic peak in plasma lidocaine concentration is likely to occur without the use of epinephrine and the

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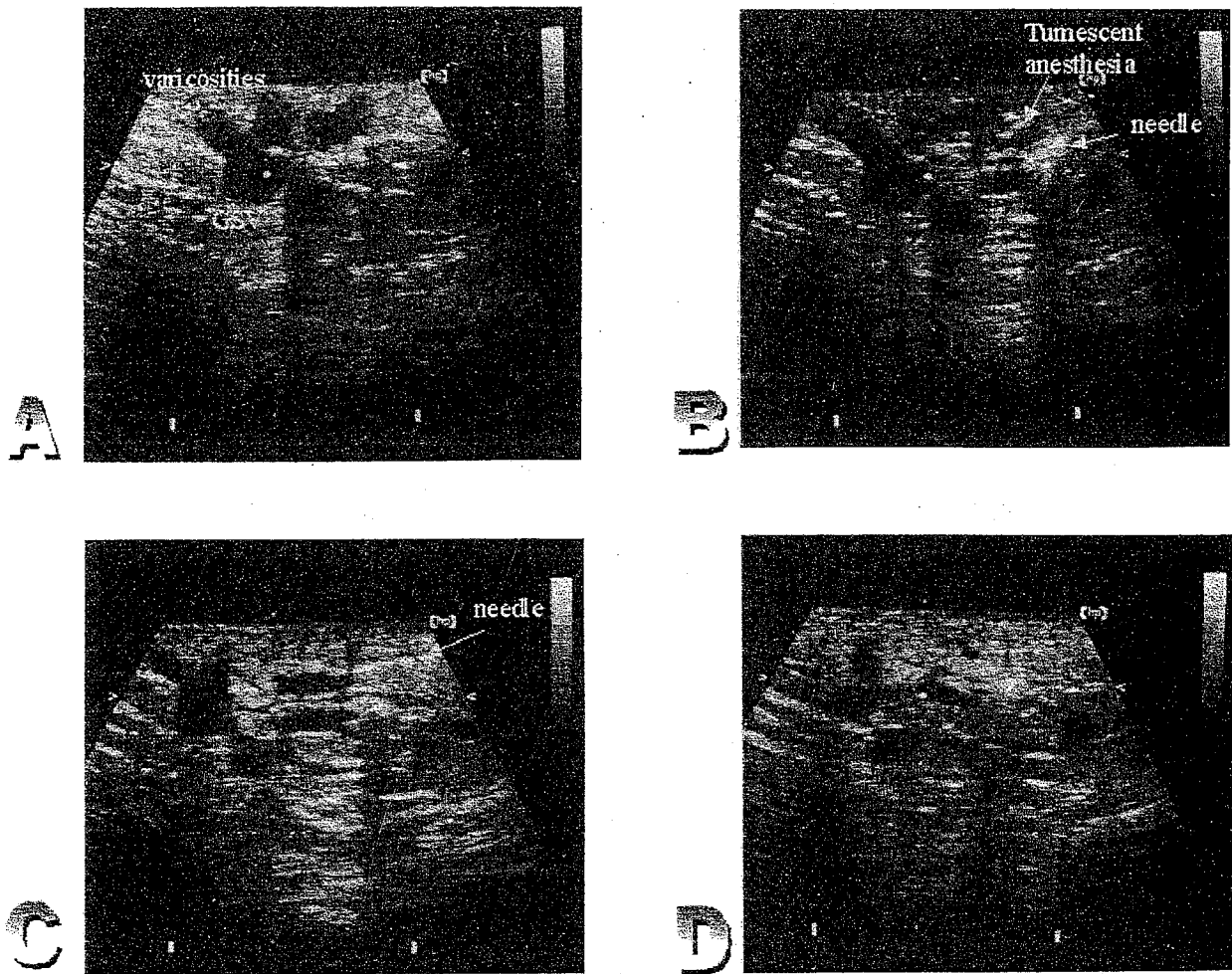


Figure 1. Tumescent anesthesia injection observed by duplex ultrasound. A) Upper calf prior to anesthesia with varicosities in the region of Dodd's perforators. Large branch varicosities originate off the greater saphenous vein (GSV) seen in transverse view. Note the defect in the superficial fascia through which the varicose veins balloon. This fascial defect can be palpated from the surface. B) Insertion of needle below the varicosities. Beginning of injection is observed as two zones of decreased density (tumescent anesthesia) ahead of the needle. C) Injection of 20 cc of tumescent anesthesia distorts the subcutaneous space with compression of many of the superficial varicosities. D) Injection completed and needle withdrawn. Tumescent anesthesia has caused virtual disappearance or compression of the superficial varicosities. Marking prior to the procedure is therefore critical. Note that the deeper veins are less affected and remain approximately the same diameter. (Figure courtesy of Robert A. Weiss, MD.)

possibility of exceeding the toxic level of lidocaine (5 mEq/dL) is increased.

Tumescent anesthesia has been applied to a variety of surgical procedures, including scalp surgery and hair transplantation, facelifts, dermabrasion, mastectomy, and simple excisional surgery.⁸⁻¹⁰ Its application to phlebectomy takes advantage of the ease of use and adds several benefits not found with local infiltration anesthesia. First, the anesthetic effect is long lasting and return of sensation occurs slowly. This contributes to the low postoperative pain scores found in our series. Second, with large volumes instilled and longer needles used, only a few needle punctures are required to completely anesthetize even long segments of veins. Third, the tumescent swelling may provide an internal com-

pression of the limb and the affected vessels. Even more importantly, the tumescence or firmness of the tissue seems to aid in "hooking" of the vein.

Duplex images of vein position during instillation of tumescent fluid are shown in Figure 1. Several actions seen here may assist in vein removal. Instillation of anesthetic fluid appears to cause separation of the vein from the surrounding subcutaneous tissue ("hydrodissection"). Additionally, superficial veins are compressed and pressed upward by the deeper fluid mass. This results in a more firm, easier to "grasp" structure near the skin surface.

Lastly, the dilute nature of the infiltrating fluid in the tumescent technique allows some inadvertent intravascular administration without consequences.

With traditional infiltrative local anesthesia it is customary to draw back with the plunger and look for a return of blood into the syringe to ensure that the needle tip is not intravascular. With the very dilute anesthetic concentration used in the tumescent technique, as long as the needle tip is not kept in one position for a prolonged period of time, there is no concern for substantial intravenous lidocaine/epinephrine administration.

In summary, tumescent anesthesia provides a very safe, easy to administer, comfortable anesthetic technique for use with ambulatory phlebectomy. Infiltrating solutions should contain epinephrine in appropriate concentrations to reduce the incidence of hematoma and induce a more gradual absorption of lidocaine into the bloodstream. The procedure requires no specialized training or expensive equipment and offers several intraoperative as well as postoperative advantages not found in traditional local anesthesia use. For these reasons, tumescent anesthesia should be considered the primary method of anesthesia in phlebectomy.

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EXHIBIT 3

EXHIBIT 3

Tumescent Anesthesia in Ambulatory Phlebectomy: Addition of Epinephrine

DOUG KEEL, DO AND MITCHEL P. GOLDMAN, MD

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BACKGROUND. The advantages of using tumescent anesthesia for ambulatory phlebectomy have recently been described. Previously, tumescent solutions have avoided epinephrine for concerns of toxicity given the large volume of anesthetic sometimes used.

OBJECTIVE. To evaluate the efficacy and safety of using epinephrine in the tumescent anesthesia solution during ambulatory phlebectomy.

METHODS. Over the course of 1 year, epinephrine in the concentration of 1:100,000 was added to the tumescent solution of patients undergoing ambulatory phlebectomy. A retrospective review of 94 sequential patients was performed to determine the rate of complications associated with the procedure.

RESULTS. The complication rate was considerably improved us-

ing tumescent lidocaine with epinephrine compared to a previously performed study of tumescent lidocaine without epinephrine. The rate of hematoma was decreased to nil while the rate of hyperpigmentation decreased from 3.6% to 0%. Overall, the rate of complications was improved when epinephrine was added to the tumescent lidocaine solution. Blood pressure measured every 5 minutes and heart rate measured continuously did not significantly change before, during or after infiltration of the anesthetic solution.

CONCLUSIONS. Epinephrine in appropriate concentrations is clearly safe when used in the tumescent anesthetic solution during ambulatory phlebectomy and should be used to reduce the incidence of hematoma and hyperpigmentation.

AMBULATORY PHLEBECTOMY is the procedure of choice for treating varicose and reticular veins from 2 to 10 cm. The advantages and disadvantages of using this procedure over sclerotherapy or standard ligation and stripping surgery have been described in detail elsewhere.¹⁻³ Smith and Goldman previously reported their experience in performing phlebectomy using tumescent anesthesia with a 0.2% lidocaine solution without epinephrine.⁴ In their retrospective review of 71 patients, they reported a 3.5% incidence of hematoma, 3.6% incidence of hyperpigmentation, and a 1.8% incidence of telangiectasia and dysesthesia. The use of tumescent anesthesia allows for maximal patient comfort and safety as opposed to general anesthesia or local anesthesia in performing ambulatory phlebectomy. In addition, tumescent anesthesia allows the patient to be ambulatory immediately after surgery.

In an effort to decrease the incidence of hematoma and provide longer-acting anesthesia, epinephrine in a 1:100,000 concentration (similar to standard liposculpture tumescent solution) was used in all patients.

Materials and Methods

Data Collection

Ninety-four sequential patients from June 1997 to May 1998 were analyzed. Chart notes and operative reports were reviewed for complications, greater saphenous vein (GSV) involvement, total volume of fluid, and type of anesthesia used. Patients were either seen in follow-up 3-14 months postoperatively or interviewed by phone by one of the authors to determine the incidence of adverse sequelae.

Anesthesia and Phlebectomy. The method for performing ambulatory phlebectomy has been described previously.⁴ The anesthetic solution was comprised of 0.2% lidocaine in normal saline solution, buffered with 1 mEq of NaHCO₃ per 100 cc of solution to which epinephrine 1:100,000 was added. Solutions were made using single-use vials of lidocaine and stock IV solutions. Infiltration was performed with 3-inch spinal needles from 22 to 25 gauge. Anesthetic solution was delivered using a peristaltic pump (Wells-Johnson, Tucson, AZ). Care was taken to keep infiltration rates below 150 cc/min. The needle was introduced into the perivenular space and infiltration begun. During infiltration, the needle was advanced as the subcutaneous space filled, and the location of the needle tip was changed often to prevent prolonged, inadvertent intravascular administration. Infiltration was completed when the area became firm or hard to the touch or the overlying skin developed a peu de orange appearance. All patients were monitored before, during, and after infiltration of the tumescent anesthesia for the duration of the procedure (20-40 minutes) with a Data-

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Scope Passport Model EL monitor (Data-Scope, Paramus, NJ). This allowed continuous display of heart rate and measurements of blood pressure every 5 minutes.

Phlebectomy was then performed in the usual manner using number 11 blades for microincisions and a variety of hooks and dissectors to facilitate vein removal. When large perforating veins or branches were encountered the stump was tied using 3-0 polygalactin-9 suture. The incisions were left open and the limb was wrapped with gauze padding and short stretch elastic bandages. Patients were seen 1 day postoperatively, and the elastic bandages replaced with a 30-40 mm Hg (Class 2) thigh-high graduated compression stocking.

Results

Women outnumbered men by more than 6 to 1 (82 to 12). The average age at time of surgery was 50 years. Follow-up periods ranged from 3 to 14 months.

The volume of anesthetic fluid ranged from 175 to 550 cc, with an average of 317 cc of fluid resulting in an average of 634 mg of lidocaine.

Blood pressure measured every 5 minutes and heart rate measured continuously did not significantly change before, during, or after infiltration of the anesthetic solution.

The number and rate of complications is listed in Table 1. The hematoma occurred in only 1 patient and was small measuring 1-2 cm in diameter, and required no intervention, resolving in 2-3 months. The largest decrease in complication rate was hyperpigmentation. There were no cases of hyperpigmentation reported using epinephrine, while the complication rate without epinephrine was 3.6%.⁴

The most common complication observed was dysesthesias. There were two patients who complained of postoperative dysesthesias ranging from numbness to burning sensations. One patient's numbness lasted 2-3 months and extended along the entire area of the extracted vein. The other patient continues to have an area of improving numbness 1 year postoperatively, which is only noticeable when she shaves her legs.

Table 1. Complications of Ambulatory Phlebectomy

Complications	With Epinephrine		Without Epinephrine ⁴
	Percent	Number	Percent
Superficial phlebitis	1.1%	1	0%
Blisters	0%	0	1.8%
Telangiectasias	1.1%	1	1.8%
Dysesthesia	2.1%	2	1.8%
Erosions	0%	0	1.8%
Hematoma	1.1%	1	3.5%
Hyperpigmentation	0%	0	3.6%

Discussion

The tumescent technique for local anesthesia during ambulatory phlebectomy has many advantages including safety, ease of administration, and patient comfort. Factors that have been previously implicated in contributing to the higher complication rate of hematoma are the lack of operator skill, the higher proportion of patients who had concomitant removal of the GSV, and the absence of epinephrine in the anesthetic fluid.⁴ Although the incidence of hematoma decreased after epinephrine was added, it is conceivable that operator skill since the initial study has improved. Additionally, a lower percentage of patients in the current study had portions of the GSV removed (17% with epinephrine compared to 27% without epinephrine). Removing the large vessel GSV may contribute to postoperative hematoma formation.

One benefit of adding epinephrine to the solution that appeared obvious was the absence of hyperpigmentation. Extravasated blood is generally considered the cause of hyperpigmentation and can lead to annoying pigment changes especially in light-skinned individuals.⁵ Presumably, the vasoconstrictive effect of epinephrine limits extravasation of blood during phlebectomy thereby reducing hyperpigmentation. Therefore, based on our positive experience, we recommend the use of tumescent anesthesia with epinephrine when performing ambulatory phlebectomy. We have encountered no adverse reactions from the use of epinephrine or from our technique of infiltration with a peristaltic pump. The only possible adverse effect would be infiltration of large amounts of lidocaine and epinephrine if the anesthetic solution was instilled into the vein lumen. Using appropriate infiltration technique and continually moving the infiltrating needle can avoid this potential complication. We have yet to encounter this problem in over 500 patients treated with this method to date.

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